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Total synthesis and biological evaluation of Tetarimycin A, (±)-Naphthacemycin A9, (±)-Fasamycin A, Benastatin A, (±)-ABX and related analogues against methicillin-resistant *Staphylococcus aureus*

Chia-Jui Lee

National Health Research Institutes, Taiwan

A rapid increase in multidrug-resistant bacteria and slow development of new antibiotics has posed a great threat to global public health. Notoriously, infection caused by *Methicillin-Resistant Staphylococcus aureus* (MRSA) has become one of the most serious problems in hospitals due to its high mortality rate. Thus, developing new antibiotics against these multidrug-resistant bacteria is urgently demanded. A class of natural products possess a gem-dimethyl tetracyclic carbon skeleton has been reported to show potent anti-MRSA activities. Among them, Fasamycins A and B were found to inhibit the FabF enzyme associated with the biosynthesis of type-II fatty acid (FASII). The other congeners (e.g., 6) not only showed activities against various MRSA, but also circumvent β-lactam resistance in combination with Imipenem. These biological features make this series of natural products become a potential hit and/or lead for further structural modifications to seek novel antibiotics. We have completed a concise total synthesis of Tetarimycin A, (±)-Naphthacemycin A9, (±)-Fasamycin A and (±)-ABX in a highly convergent manner using efficient anion annulation in the last stage. With reductive olefin coupling, intermolecular Friedel-Crafts acylation and Suzuki-Miyaura coupling as key operations, these synthetic approaches become economic and general for potential antibiotics possessing a linear tetracyclic carbon skeleton.

Biography

Chia-Jui Lee completed his PhD from National Taiwan Normal University in 2016. He is currently a Post-doctoral in the area of new drug development in the Institute of Bio-technology and Pharmaceutical Research, National Health Research Institutes in Taiwan.

roylee8819@gmail.com

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